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EXAMINER	
OGUNBIYI, OLUWATOSIN A	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,583	VOUSDEN, KATHERINE ANN	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,14-16 and 18-35* is/are pending in the application.

4a) Of the above claim(s) *1,14 and 18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8 and 23-35* is/are rejected.

7)☒ Claim(s) *8, 30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 3/11/08 has been entered into the record. Claims 2-7, 9-13 and 17 are cancelled. Claims 23-35 are added. Claims 1,8, 14-16 and 18-35 are pending. Claims 1, 8, and 23-35 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Applicant is advised that should claims 23-26 be found allowable, claims 30-32 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objection Withdrawn

The objection to claim 8 is withdrawn.

New Claim Objections

Claim 8 line 8 please insert 'one' after 'said'.

Claims 30 and 31 the spelling of assay is misspelled.

Rejections Withdrawn

The rejection of claim 1 under 35 U.S.C. 102(e) as being anticipated by Weinstock et al. US 6,747,137 B1 published Jun. 8, 2004, filed Feb 12, 1999 is withdrawn in favor of a new rejection set forth below.

Rejections Maintained

The rejection of claim 8 and newly added claims 27-29 and 33-35 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons made of record in the previous office action mailed 12/27/2007.

Applicants' arguments and the response:

Applicant asserts that one of ordinary skill in the art, on reading the application, would readily appreciate that the assay for CCA1 activity that is fully described in Example 3, using CCA1 protein produced and purified as taught in Examples 1 and 2 of the specification would readily allow one to determine whether a compound tested for its effect on growth or viability of cells expressing *C. albicans* CCA1 was an inhibitor of CCA1.

Applicant's arguments have been carefully considered in full but are not persuasive.

The assay described in example 3 is an assay for determining the activity of CCA1 protein. Although, one can use this assay to determine the direct effects of a compound on CCA1 protein, the claim, however is drawn to cell based screening or testing for candidate anti-fungal. The claims do not recite that the CCA1 protein is purified and does not recite that the effect of a compound on purified CCA1 activity is determined. Thus, Applicants arguments are not

commensurate with the scope of the claims. The claims as written are clearly drawn to a cell bases screening or testing for candidate anti-fungal compounds and not to a screening or testing for candidate anti-fungal compounds that directly impair CCA1 protein activity.

New Rejections

Claim Rejections - 35 USC § 112

Claims 8 and 27-29 and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 8 is drawn to a method of screening or testing for candidate anti-fungal compounds that impair *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) activity-comprising:

a) providing a C. *albicans* cell wherein the cell expresses *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) under the control of a heterologous promoter;

b) providing one or more candidate compounds;

c) contacting said *Candida albicans* cell(s) with said or more candidate compounds;

d) determining whether the candidate compound

inhibits growth or viability of the cell(s); and

e) determining whether the candidate compound is a CCA1 inhibitor.

Applicant points to the specification p. 5 lines 22-35 and examples 1-3 p. 9-10 for support for amended claim 8.

The above method of cell based screening or testing for candidate antifungal compound with the particular method steps a-e is not disclosed in the specification. Page 5 lines 22-35 does not disclose the above method with step 'e'. Example 1 and 2 in the specification is drawn to expression and purification of CCA1. Example 3 discloses an in vitro assay for determining CCA1 activity and does not disclose the method of claim 8 with steps a-e. Thus, the amendment to claim 8, particularly step e is deemed new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstock et al. US 6,747,137 B1 published Jun. 8, 2004, filed Feb 12, 1999 (cited in previous action) in view of Onishi et al. Antimicrobial Agents and Chemotherapy, Feb 2000, p. 368-377 (cited in previous action).

The claims are drawn to a method of screening or testing for candidate anti-fungal compounds that impair Candida albicans ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) activity

comprising:

a) providing fungal Candida albicans CCA 1;

b) providing one or more candidate compounds;

c) contacting said CCA 1 with said one or more candidate compounds; and

d) determining the ability of the candidate compound to inhibit CCA1 activity.

Weinstock et al teach a method of screening test compounds for anti-fungal activity comprising providing a *Candida albicans* target polypeptide sequence such as *Candida albicans* tRNA nucleotidyl transferase also known as CCA1 (table 2 columns 587 and 588 contig3807) and contacting a test compound with said CCA 1 and selecting those which bind to said target sequence as anti-fungal candidates (See column 10 lines 28-45, column 20 lines 46-67 to column 21 lines 1-54 (for description of table 2 which discloses *Candida albicans* CCA1).

Weinstock et al does not specifically disclose determining the ability of the candidate compound to inhibit CCA1 activity.

Onishi et al teaches a method for screening or testing candidate anti-fungal compounds in vitro by determining that said candidate anti-fungal inhibit the activity of a target *C. albicans* protein. Onishi et al also teach method for screening or testing candidate antifungal compounds by determining the effect of said compounds on growth and viability of *C. albicans* cells (page 369 column 1 materials and methods and table 1, page 370 column 2 first full paragraph, page 373 column 1 – 2 and table 4).

Although, Weinstock et al does not specifically disclose determining the ability of the candidate compound to inhibit CCA1 activity, it is prima facie obvious to one of ordinary skill in the art at the time that the instant invention was made that determining the binding of a compound to protein such as CCA1 to determine whether it is a anti-fungal candidate necessarily involves the determination that the candidate compound inhibits (or does not inhibit) the activity of said protein as taught by Onishi et al who teach a method for screening or testing candidate anti-fungal compounds in vitro by determining that said candidate anti-fungal inhibit the activity of a target *C. albicans* protein.

Applicant's arguments against the Weinstock et al reference

Applicant argues that Weinstock et al disclose a method for screening test compounds for anti-fungal activity by selecting an essential fungal specific sequence and testing which compounds bind to it (column 10, lines 46-47) but that Weinstock et al does not disclose the

CCA1 gene from Candida as an essential gene and that the extensive list of open reading frames in Weinstock et al does not qualify as a target sequence to be assayed for anti-fungal activity.

Applicant's argument is carefully considered but is not found persuasive. First, column 10 lines 46-47 of Weinstock et al does not teach a method for screening test compounds as asserted. Column 10 lines 46-47 is drawn to methods for preventing or treating disease. Second, one of skill in the art would recognize CCA1 as an essential gene in general. CCA1 (ATP (CTP): tRNA nucleotidyltransferase) also known amongst many synonyms as tRNA nucleotidyltransferase or CCA-adding enzyme is a ubiquitous enzyme that catalyzes the incorporation of CMP and AMP into incomplete tRNA chains. The enzyme is required for normal growth of cells and is involved in repair of tRNA molecules that are missing part of the 3' terminus. (See introduction of Navarro et al. 1991, Italian Journal Biochemistry; 40(5) pages 295-303 and review article, Weiner, 2004. Current Biology, vol. 14, issue 20 pages R883-R885, both cited previously). Further, Hanic-Joyce et al (Yeast 2002: 19:1399-1411, cited in IDS) teach that mutations of essential residues in CCA1 is lethal to *Candida glabrata* (p. 1406 column 2). Thus, since the enzyme is required for normal growth of cells and has been shown to be essential for *C. glabrata*, said CCA1 of *C. albicans* is expected to also be essential for the normal growth of the fungi.

As to Applicant's reference to the extensive list of open reading frames disclosed by Weinstock et al, the use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006,1009, 158

USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including non-preferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied,493 U.S. 975 (1989).

Applicant argues that Weinstock et al does not make any mention of CCA1 activity much less disclose assays for CCA1 activity. Applicant's argument is carefully considered but is not persuasive. As set forth above, although Weinstock et al does not specifically disclose determining the ability of the candidate compound to inhibit CCA1 activity, it is prima facie obvious to one of ordinary skill in the art at the time that the instant invention was made that determining the binding of a compound to protein such as CCA1 to determine whether it is an anti-fungal candidate necessarily involves the determination that the candidate compound inhibit (or does not inhibit) the activity of said protein. See Onishi et al (above) who teach a method for screening or testing candidate anti-fungal compounds in vitro by determining that said candidate anti-fungal inhibit the activity of a target *C. albicans* protein. The point of testing whether a compound is an anti-fungal candidate using a direct test of said compound on a fungal protein is to determine whether the compound inhibits the activity of the protein. As to assays, this argument is not commensurate in scope with the claim 1 as claim 1 does not disclose any particular assay for CCA1 in the method steps.

Claims 23-26 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstock et al. US 6,747,137 B1 published Jun. 8, 2004, filed Feb 12, 1999 (cited in previous action) and Onishi et al. Antimicrobial Agents and Chemotherapy, Feb 2000, p. 368-377 (cited

in previous action) as applied to claim 1 further in view of Chen et al (The Journal of Biological Chemistry, 1990, vol. 265, p.16221-16224, cited in IDS).

The combination of Weinstock and Onishi et al is set forth supra. Said combination does not teach a tRNA nucleotidyl transferase assay for determining the ability of the candidate compound to inhibit CCA1 activity.

Chen et al teach an assay for measuring tRNA nucleotidyltransferase activity (aka CCA1) i.e. a tRNA nucleotidyl transferase assay which uses a labeled/radiolabeled nucleotide (3H-CTP).

It would have been prima facie obvious to one of ordinary skill in the art to use the enzymatic assay disclosed by Chen et al for determining the activity of CCA1 (tRNA nucleotidyltransferase) in the method of Weinstock et al and Onishi et al as combined. The enzymatic assay for determining the activity of CCA1 is known in the art and it would have been within the skill of the ordinary artisan to adopt or adapt said enzymatic assay for determining the activity of CCA1 in the presence of a candidate anti-fungal compound.

Claims 8, 27-29 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Georgopapadakou et al. Expert Opin. Investig. Drugs (2002) 11 (8):1117-1125 in view of Weinstock et al. US 6,747,137 B1 published Jun. 8, 2004, filed Feb 12, 1999 (cited in previous action) and Nakayama et al. Infection and Immunity , Dec. 2000, p. 6712-6719 and Onishi et al (Feb. 2000, Antimicrobial Agents and Chemotherapy p. 368-377, cited previously).

The claims are drawn to a method of screening or testing for candidate anti-fungal compounds that impair *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) activity-comprising:

a) providing a C. *albicans* cell wherein the cell expresses *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) under the control of a heterologous promoter;

b) providing one or more candidate compounds;

c) contacting said *Candida albicans* cell(s) with said or more candidate compounds;

d) determining whether the candidate compound inhibits growth or viability of the cell(s); and

e) determining whether the candidate compound is a CCA1 inhibitor.

Weinstock et al teach a method of screening test compounds for anti-fungal activity comprising providing a *Candida albicans* target polypeptide sequence such as *Candida albicans* tRNA nucleotidyl transferase also known as CCA1 and contacting a test compound with said CCA 1 and selecting those which bind to said target sequence as anti-fungal candidates (See column 10 lines 28-45, column 20 lines 46-67 to column 21 lines 1-54 (for description of table 2 which discloses *Candida albicans* CCA1).

Weinstock does not teach a method for screening or testing candidate antifungal compounds that impair said CCA1 activity comprising a) providing a C. *albicans* cell wherein the cell expresses *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) under the control of a heterologous promoter; b) providing one or more candidate compounds; c) contacting said *Candida albicans* cell(s) with said or more candidate compounds; d) determining whether the candidate compound inhibits growth or viability of the cell(s); and e) determining whether the candidate compound is a CCA1 inhibitor.

Georgopapadakou et al teach a cell based screening for candidate inhibitors of a *C. albicans* enzyme using a *C. albicans* tetracycline inducible/regulatable promoter system which comprises providing said *C. albicans* expressing said enzyme under said tetracycline inducible/regulatable promoter (p. 1121 column 1 last paragraph).

Nakayama et al teach said tetracycline regulatable system of gene expression in *C. albicans* which uses a tetracycline inducible heterologous tet promoter (see p. 6712 column 1 to column 2, p. 6713 column 1 and column 2 – materials and methods). Nakayama et al teach inducible gene expression in the absence of doxycycline or tetracycline (p. 6712 column 2 first incomplete paragraph and p. 6715 first column) and teach repression of the promoter in the presence of tetracycline or doxycycline thus resulting in inhibition of gene expression ((p. 6712 column 2 first incomplete paragraph and p. 6715 first column to second column).

Onishi et al teaches a cell based screen for antifungal activity of several compounds (which putatively inhibit a fungal enzyme) by a growth inhibition assay on *C. albicans* (page 369

column 1 materials and methods and table 1) and then the compounds were evaluated to determine whether said compounds were direct inhibitors of said enzyme by measuring the enzyme's activity in the presence of said compounds (page 370 column 2 first full paragraph, page 373 column 1 – 2 and table 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to screen for candidate compounds that impair the activity of *C. albicans* CCA 1 disclosed by Weinstock et al using the methods disclosed by Georgopapadakou et al and Nakayama et al and Onishi et al because Georgopapadakou et al teach that a cell based screening method using tetracycline inducible/regulatable gene expression in *C. albicans* can be used to screen for inhibitors of a *C. albicans* enzyme and Nakayama et al teach said method of tetracycline regulatable system of gene expression in *C. albicans* which uses a tetracycline inducible heterologous tet promoter. It is obvious that said cell based screening method will involve the determination of the effect of said compound on the growth and viability of said *C. albicans* (since the method is directed at cell based screening for an antifungal compound) and it would be prima facie obvious to compare the growth or viability of said *C. albicans* when the tet promoter is repressed (no CCA1 expression) as a control to determine any differences in the effect of compounds on the growth or viability of *C. albicans* in the presence or absence of CCA1 expression.

Further it is obvious that validation tests are further carried out to determine that said candidate antifungal compound inhibits CCA1 activity directly as taught by Onishi et al who teaches a cell based screen for antifungal activity of several compounds (which putatively inhibit an enzyme's activity) by a growth inhibition assay (page 369 column 1 materials and

methods and table 1) and then the compounds were evaluated to determine whether said compounds were direct inhibitors of the enzyme by measuring the enzyme's activity in the presence of said compounds (page 370 column 2 first full paragraph, page 373 column 1 – 2 and table 4).

Status of Claims

Claims 1, 8, and 23-35 are rejected. No claims allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645